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WO 98/57738 A1
US 5398806 A

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(54) Abstract Title
Reaction station with reactor vessel support

(57) A chemistry reaction station 11 has a base unit 12 with a heater block 13 having a plurality of recesses 14 for reaction vessels 1. The vessels are releasably held in fixed position relative to the block by a mounting 16, which also includes mounting facilities for an accessory used in the reaction. As described, each vessel 1 is a closed bottom glass tube having an integral condenser 4 and a ground glass connector (3, Fig 1) at the top. The mounting also has a support 22 for a nitrogen supply manifold, a support 27 for nitrogen bubblers 28, and a manifold 29 for supplying and withdrawing cooling fluid to the condensers. The mounting is held by screws 18-20 and can be removed as a whole from the block, together with the vessels it supports. The block may include magnetic stirring means.

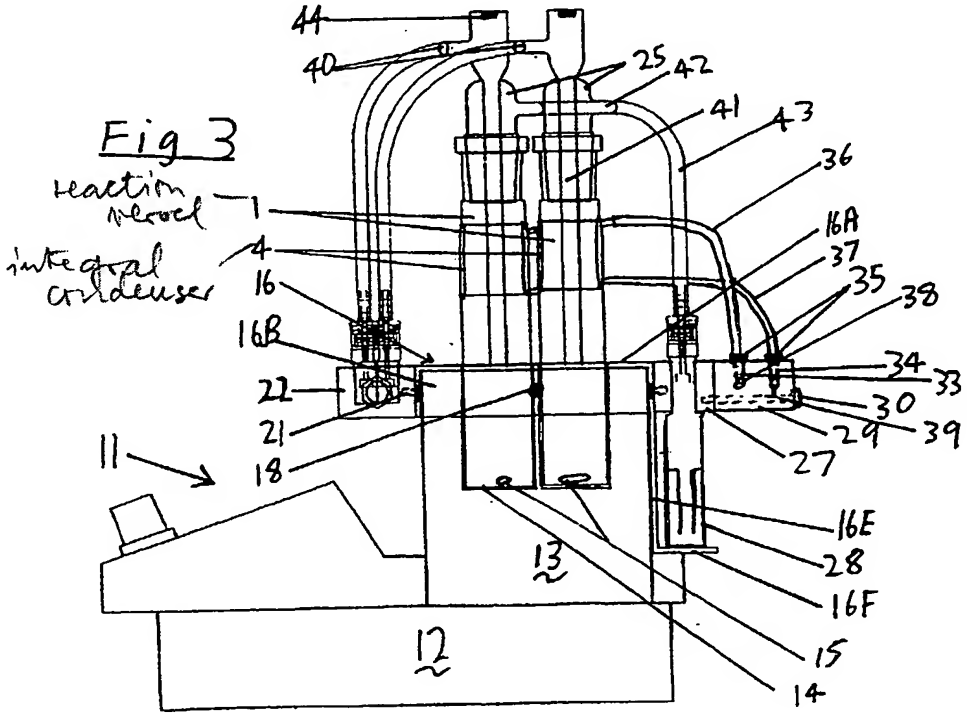

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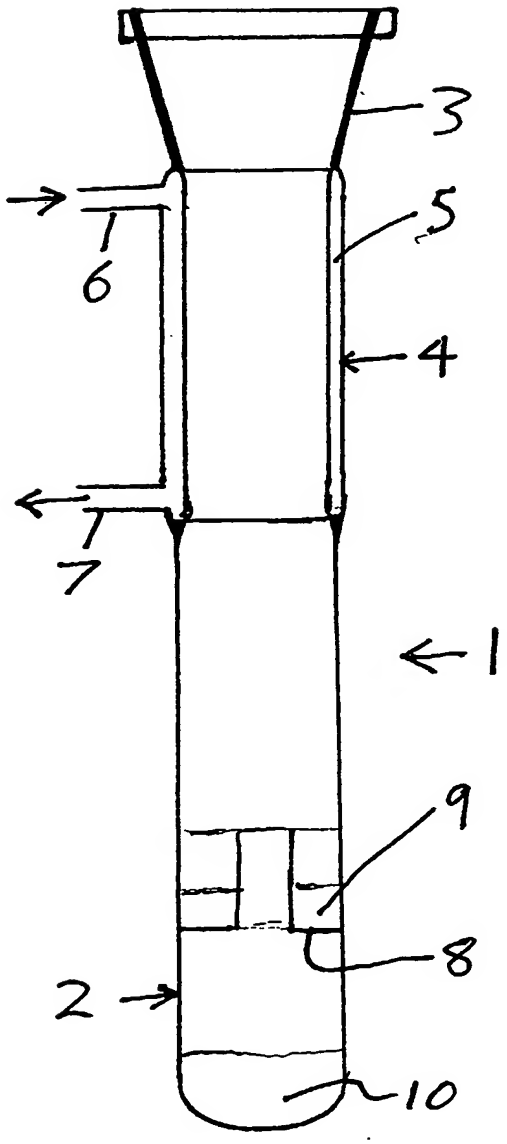
Fig 1



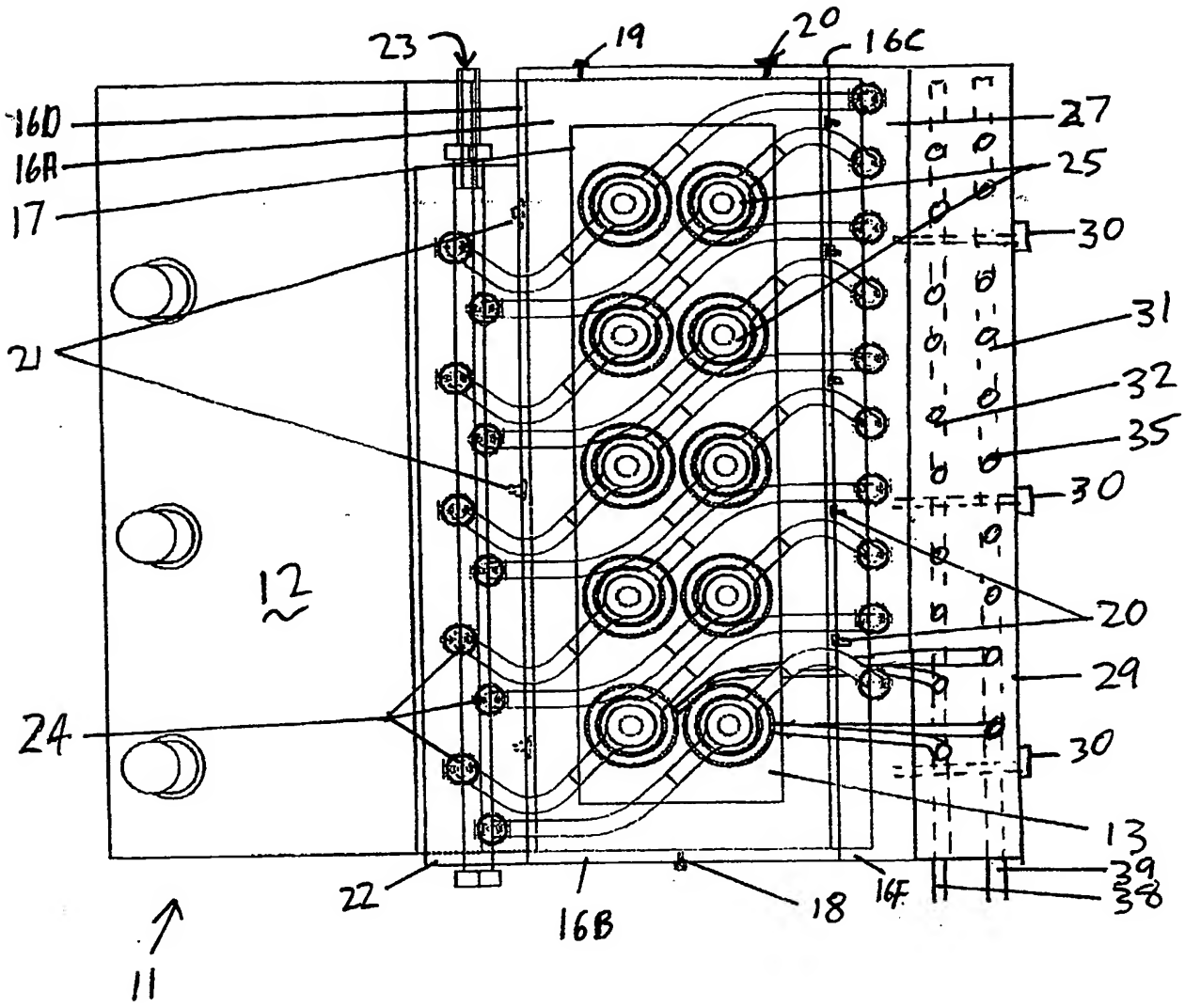
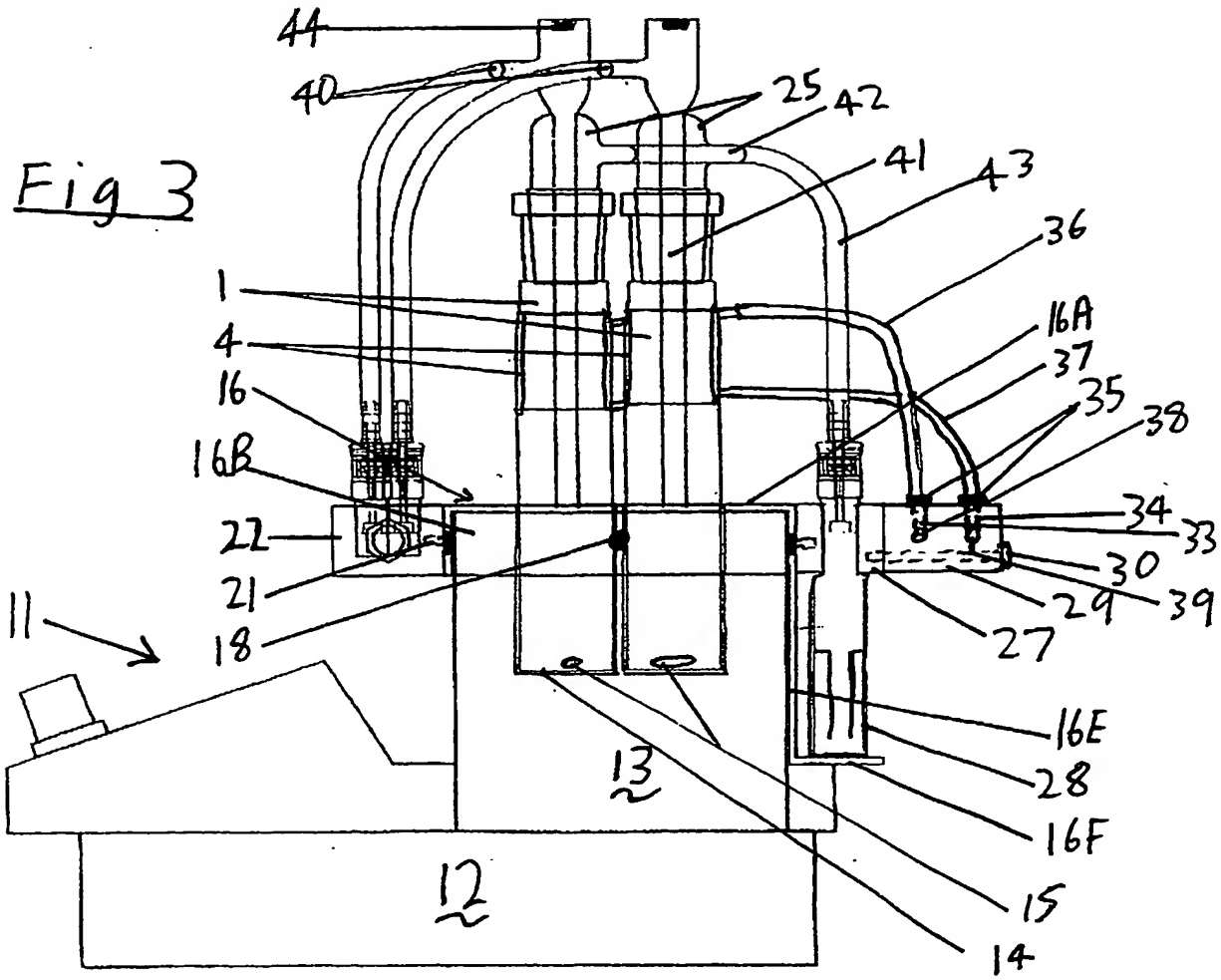


Fig 3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CHEMISTRY REACTION STATION AND REACTION VESSEL THEREFOR

A first aspect of the present invention relates to a chemistry reaction station and particularly, but not exclusively, to the type comprising a heater and a stirrer mechanism for a plurality of reaction vessels, normally in the form of test tubes. A second aspect of the invention relates to a reaction vessel particularly but not exclusively suitable for use with a reaction station.

Present trends in modern chemistry require reactions to be carried out in parallel in a plurality of reaction vessels maintained at the same temperature, this is referred to as combinatorial chemistry and is used to perform organic synthesis. A piece of laboratory equipment developed to fulfil this requirement for example is the reaction station disclosed in WO 99/13988. This comprises a carousel arranged to receiving a plurality of reaction vessels in an aluminium block, which block is placed on a conventional hot plate and magnetic stirrer device.

Another type of commonly available reaction station is that provided by STEM Corp. Ltd, this comprises a self contained unit designed to stand on the laboratory bench top and has a heating block with ten receptacles for receiving appropriately dimensioned reaction vessels in the form of test tubes. A rotating magnet under each receptacle cooperates with a magnetic stirrer located in each reaction vessel which follows the magnet in order to stir the contents of the reaction vessel during the reaction.

These two prior art devices provide a way of heating or stirring reagents within a glass reaction vessel and for enabling a plurality of reaction vessels to be treated in a similar manner. However, in addition to heating and stirring the contents of a reaction vessel there is often a requirement to cool the upper portion of the reaction vessel in order to condense or to reflux, reagent and/or solvent which may evaporate or boil during the reaction. There is also additionally often a requirement to exclude air by flowing N_2 over the top of the reaction vessels.

In WO99/13988 there is a disclosed an upper stage through which each reaction vessel extends, which stage is cooled by a cooling fluid in order to cool the upper portion of each reaction vessel. There is also a common gas supply leading to a number of outlets each with a connection hose to a cap to be placed over each reaction vessel. through which caps N_2 gas can flow. However, with this arrangement the thermal contact between the upper stage and the reaction vessels is less than perfect.

Referring now to the reaction station marketed by STEM Corp Ltd, this is preferred by some chemists and there are many already in existence. In order to permit refluxing with the reaction station a device has been developed termed a "cold finger" and this is disclosed in WO99/08767. This comprises a combined laboratory condenser and vessel connector for placing in a specially designed reaction vessel suitable for use with the STEM Corp Ltd reaction station. The reaction vessel has a connector provided at its upper end for receiving the "cold finger". The "cold finger" comprises a, normally glass, double walled tube which extends into the reaction vessel and through which cooling fluid can be conveyed so that there is a "cold finger" extending into the reaction vessel. There are also connections through which

N_2 can be flowed across the top of the tube extending down the centre of the cold finger.

The cold finger disclosed in W099/08767 has four primary connections, a cooling fluid inlet, a cooling fluid outlet, an N_2 inlet and an N_2 outlet. A STEM Corp Ltd reaction station will typically comprise ten wells for receiving ten reaction vessels. If each of these has a cold finger associated with it this results in forty connections. To minimise the number of supply lines "cold fingers" can be arranged in series, N_2 flowing from one vessel to another. This though could potentially cause a problem with cross contamination and also means that the "cold finger" can not be removed from one reaction vessel without first having to stop the flow to all reaction vessels. There is also then the possibility of letting air in while the supply line is disconnected.

It is an object at the present invention to provide an improved reaction station and reaction vessel therefor.

According to a first aspect of the present invention there is provided a chemistry reaction station comprising: a base unit having a heating block with a plurality of recesses therein arranged to receive reaction vessels; and a mounting for accessories used in connection with the performance of reactions in the reaction vessels, the mounting being arranged to releasably support the accessories in fixed positional relationship to the heating block.

A reaction station in accordance with the first aspect of the present invention provides a mounting through which various accessories can be attached to the reaction station.

This enables the reaction station itself to become a fixed platform for ancillary equipment associated with reactions taking place in the reaction vessels and avoids the need to precariously arrange items about the reaction station in an unsecured manner which too often results in stressed or broken connections or components caused by movement of the components. It also makes it difficult, if not impossible, to remove the reaction station with the accessories in situ. In contrast with the reaction station in accordance with the first aspect of the present invention, the reaction station can be moved without interfering with the reactions taking place.

Preferably the mounting is arranged to support different types of accessories by means of common fixings. In this way a common mounting can be used to customise a reaction station to perform different reactions requiring the use of different accessories.

In addition to the reaction station having a heating block, the base unit will typically comprise a stirrer mechanism for activating any magnetic stirrers placed in the reaction vessels.

The invention is particularly advantageous when the reaction station comprises at least one accessory, the one accessory comprising a manifold having an inlet and a plurality of outlets. Alternatively, or in addition thereto, the one accessory may comprise a manifold of having at least one outlet and a plurality of inlets. This enables one inlet and/or outlet from a common supply, or to a common return, to be connected to a plurality of reaction vessels located in the recesses of the base unit heating block, permitting an individual connection to be made to each reaction vessel or associated

component, which connections can all be made in parallel avoiding the need for connection in series.

Preferably the plurality of outlets and/or the inlets corresponds to the number of recesses in the heating block and outlet and/or inlet is provided for each reaction vessel.

It is particularly advantageous if each of the plurality of outlets and/or inlets can be independently sealed, this enables one reaction vessel to be removed from the reaction station without the need to interfere with the other reaction vessels, and preferably each of the plurality of outlets and/or the plurality of inlets is arranged to receive a connecting tube to a reaction vessel and to be self sealing on removal of the connecting tube. This permits removal of a reaction vessel simply by lifting it out of its recess in the heating block whilst simultaneously pulling any connections from the manifolds. A further advantage of this is that the self sealing mechanism on the manifold ensures that the fluid within the manifold cannot escape or become contaminated with air, for example if this is inert an gas such as N_2 supplying all the reaction vessels this supply can not be contaminated by air as the self sealing mechanism automatically closes the inlet or outlet on removal of the tube.

Preferably the reaction station comprises of a number of reaction vessels each having a cooling fluid inlet and a cooling fluid outlet for connecting to respective ones of the plurality of outlets and/or plurality of inlets of one or more of the manifolds. This arrangement permits cooling fluid to be supplied to and from each reaction vessel directly without the requirement to have ancillary components mounted on top of the

reaction vessels, which can be easily damaged. Such an arrangement is made particularly practical by the provision of common manifolds enabling a local connection via the manifolds to both a cooling fluid source and cooling fluid return, the manifolds being maintained in fixed positional relationship to the reaction station in which each reaction vessel is mounted.

Depending on the application to which the reaction station is put, it may be preferable that the reaction station comprise a manifold having an inlet connected to an inert gas supply. The outlets can then be connected to each reaction vessel providing an independent inert gas supply to each reaction vessel avoiding any possibility of cross contamination.

It is particularly advantages if the reaction station comprises the plurality of reaction vessels and a plurality of reaction vessel head portions each mounted to an upper open end of a reaction vessel, each head portion being connected to an inert gas supply manifold. Each head portion may have an extension tube, extending within the reaction vessel. the said extension tube arranged to cause inert gas to be flushed through the reaction vessel.

Additionally, each reaction vessel head may have a septa entry into the said extension tube through which reagents can be added to the tube. Also the reaction station may additionally comprise a plurality of N_2 bubblers mounted on the mounting. Each of these can be used to independently receive the N_2 gas flowing through the reaction vessels, the N_2 bubblers ensuring air can not return to the system. The provision of an

individual bubbler for each reaction vessel ensures that no cross contamination can take place and permits removal of one reaction vessel without disturbing the others.

It is particularly advantageous if the reaction station has a mounting which comprises a bracket releasably attached to the base unit. This may enable the bracket to be retrofitted to the many existing reaction stations or may enable different types of bracket to be fitted depending on the type of reaction to be performed and the accessories required.

Advantageously, the mounting is arranged to be removable from the said base unit, when the said base unit has a plurality of reaction vessels located therein and when the bracket has a accessories mounted thereon. This permits a bracket with associated accessories for a particular type of reaction to be simply lifted off and another bracket with appropriate accessories for another stage of the reaction to be substituted therefor. Alternatively it permits a bracket to be transferred to another reaction station. Thus a bracket may be set up for a particular reaction and may simply be taken "off the shelf" and fitted to a appropriate reaction station when a particular reaction is desired to be performed.

According to a second aspect of the invention there is provided a mounting bracket for a reaction station in accordance with the first aspect of the invention and/or a range of mounting brackets for use with such a reaction station, each bracket arranged to mount different accessories or combinations of accessories to said reaction station.

According to a third aspect of the present invention there is provided a reaction vessel having a closed lower end and open upper end, the vessel comprising in an integral condenser. Employing this aspect of the present invention enables a reaction to take place in a reaction vessel and condensation or reflux of the reagent or solvent to take place in that reaction vessel without the requirement to provide an ancillary piece of equipment. This would typically have been an additional stage placed about a conventional reaction vessel or a separate component connected to the top of a conventional reaction vessel, the latter tending to make the arrangement particularly tall and prone to accidental damage.

The integral condenser preferably comprises of a double walled tubular section having an inlet and an outlet through which cooling fluid can flow, passing through a cavity formed by the double walled section. This permits the vessel to have a conventional tubular form and be used in standard reaction stations, the dimensions of the vessel not being greatly in excess of those of a standard vessel.

The reaction vessel preferably has a connection portion forming the open upper end for connecting to additional equipment. The vessel is preferably formed entirely of glass with its connector comprising a ground glass connection.

Depending on the application to which the vessel is to be put it may advantageously comprise a head portion for mounting on the open upper end, the said head portion having an inlet for receiving inert gas. Preferably the head comprises an extension tube which, when the head is mounted on said upper opening, extends into the vessel permitting inert gas such as N_2 to be flowed through the vessel expelling all air.

The head may comprise a septa through which reagents or solvents and the like may be added or removed to or from the reaction vessel. The septa preferably opens into the top of the said extension tube permitting reagents to be added through the extension tube.

One embodiment employing all aspects of the present invention will now be described by way of example only with reference to the accompanying figures of which:

Figure 1 is a side elevation of a reaction vessel in accordance with the third aspect of the present invention;

Figure 2 is a plan view of a reaction station in accordance with the first aspect of the present invention; and

Figure 3 is a side elevation of figure 2.

Referring to figure 1 reaction vessel indicated generally as 1 is formed from laboratory glass and is substantially cylindrical in form, comprising a lower closed end having a diameter slightly less then that of a standard aperture in a reaction station (such that it fits closely in an aperture in a reaction station and is maintained upright by the reaction station). At its upper end the reaction vessel comprises a ground glass connection portion 3 for receiving further fitting which may for example be a reaction vessel head, described below with reference to figures to 2 and 3, a "Dean and Stark"

device used for removing water, a dropping funnel or any such similar apparatus that it is desired to connect to the reaction vessel.

The reaction vessel has around its mid portion a condenser 4 formed between a double walled portion of the tube which forms a cavity 5. Cooling fluid is received at inlet 6 and circulates through cavity before exiting outlet 7. The condenser is used for condensing solvent or reagents so that they return to the reactant in the lower part of the vessel.

Although not normally employed the vessel may optionally contain a well 8 for catching condensate 9 which evaporates, condenses on the condenser and runs down the side of the tube into the well 10. This arrangement will only be applicable to particular types of reactions.

Referring to figures 2 and 3 a reaction station, indicated generally as 11, which could be any appropriation reaction station, (the one illustrated is manufactured by Stem Corp Limited of Tollesbury, United Kingdom). The reaction station comprises a base unit 12 having a heating block 13, with a plurality of recesses 14 therein.

In each recess 14 there is a reaction vessel 1, of the type illustrated in figure 1. In the bottom of each reaction vessel is a plastic coated metallic stirrer 15 which is caused to rotate and stir the contents of the vessel by means of mechanically propelled magnets in the heater block 13. These are not shown this being well known and standard apparatus.

On top of the heating block 13 of the reaction station 11 is mounted a bracket 16 formed out of flat steel plate having an upper portion 16A with an aperture 17 therein, (through which the ten reaction vessels 1 protrude), side skirts 16B and 16C, a side skirt 16D and a side skirt 16E having a foot plate 16F.

The bracket 16 is mounted to the reaction station heating block 13 by means of screws 18, 19 and 20. When these are partially released and the various connections removed from the reaction vessels the bracket and accessories may simply be lifted off the reaction station with the reaction vessels in place if desired.

Mounted to the bracket 16 by recessed screws 21 is a first manifold 22 having an inlet 23 for receiving an inert gas, such as N_2 and a plurality of outlets 24 providing supplies of N_2 to reaction vessel heads 25 discussed below.

On the other side of the bracket 6, and secured by recessed screws 20 is an N_2 bubbler support block 27 which comprises a machined PTFE block having a plurality of apertures therein which support N_2 bubblers 28. These bubblers also rest on foot plate 16F. The N_2 bublers receive the N_2 from the reaction vessel heads and prevent air

returning to the reaction vessel. Secured to the bubbler support 27 is a further manifold 29 secured by screws 30. This manifold also again comprises a machined PTFE block having 2 axially extending bores 31 and 32 each connected respectively to ten passages 33 and 34 which terminate on top of support block 27 in self sealing valves 35. These valves 35 remain closed until tubes 36, 37 are pushed in to them. The manifold 29 has an inlet 38 for receiving cooling fluid which passes through tube 36 to condenser 4 and returns via tube 37 to outlet 39.

To the top of all each reaction vessel 1 is mounted a reaction vessel head 25 each head comprising an inlet 40 for receiving N_2 gas which passes down extension tube 41. flowing out over the surface of any reactant and back up the reaction vessel to be expelled via outlet 42. From here it is conveyed by pipe 43 to N_2 bubler 28. On the top of each inlet 40 is a septa 44 through which reagents may be added or removed by pipette through the extension tube 41.

The invention has been described above with reference to one embodiment only. It will be apparent to one skilled in the art that any number of brackets to attach to different types of reaction stations may be designed in accordance with the present invention as defined by the claims. Furthermore, specific brackets may be manufactured for specific purposes, for example in the embodiment illustrated a bracket is shown specifically designed to hold N_2 bubblers. Similarly any number of accessories can be bolted on to the bracket, or indeed to any other mounting on the reaction block. Similarly various variations on the illustrated reaction vessel will occur to one skilled in the art.

CLAIMS

1. A chemistry reaction station comprising: a base unit having a heating block with a plurality of recesses therein arranged to receive reaction vessels; and a mounting for accessories used in connection with the performance of reactions in the reaction vessels, the mounting being arranged to releasably support the accessories in fixed positional relationship to the heating block.

2. A station as claimed in claim 1 wherein the mounting is arranged to support different types of accessories by means of common fixings.

3. A station as claimed in claim 1 or 2 wherein the base unit comprises a stirrer mechanism for activating any magnetic stirrers in the reaction vessels.

4. A station as claimed in claim 2 or 3 including at least one accessory the one accessory comprising a manifold having an inlet and a plurality of outlets.

5. A station as claimed in any preceding claim including at least one accessory, the one accessory comprising a manifold have at least one outlet and a plurality of inlets.

6. A station is claimed in claim 3 or 4 wherein the plurality of outlets and/or the plurality of inlets correspond to the number of recesses in the heating block.

7. A station as claimed in claim 4, 5 or 6 wherein each of the plurality of outlets and/or the plurality of inlets can be independently sealed.

8. A station as claimed in claim 7 wherein each of the plurality of outlets and/or the plurality of inlets is arranged to receive a connecting tube to a reaction vessel and to be self sealing on removal of the connecting tube.

9. A station as claimed in any one of claims 5 to 8 comprising a number of reaction vessels each having a reflux portion having a cooling fluid inlet and a cooling fluid outlet for connecting to respective ones of the plurality of outlets and plurality of inlets of one or more of the manifolds.

10. A station as claimed in any preceding claim comprising a manifold having an inlet, connected to an inert gas supply, and a plurality of outlets.

11. A station as claimed in claim 10 comprising a plurality of reaction vessels and reaction vessel head portions, each head portion mounted to an upper open end of a reaction vessel, each said head portion being connected to the inert gas supply manifold.

12. A station as claimed in claim 11 wherein each head has an extension tube extending within the reaction vessel said extension tube arranged to cause inert gas to be flushed through the reaction vessel.

13. A station as claimed in claim 12 wherein each head has a septa entering into said extension tube.

14. A station as claimed in any preceding claim comprising a plurality of N_2 bubblers mounted on the mounting.

15. A station as claimed in any preceding claim wherein the mounting comprises a bracket releasably attached to the base unit.

16. A station as claimed in claim 15 wherein the mounting is arranged to be removable from said base unit when said base unit has a plurality of reaction vessel located therein and when the bracket has plurality of accessories mounted thereon.

17. A mounting bracket for a reaction station as claimed in any preceding claim.

18. A range of mounting brackets for use with a reaction station as claimed in any preceding claim, each bracket arranged to mount different accessories, or combinations of accessories to said base unit.

19. A reaction block substantially as hereinbefore described with reference to, and/or as illustrated in, one or more of the accompanying figures.

20. A mounting brackets for a reaction block the mounting being substantially as hereinbefore described with reference to, and/or as illustrated in, one or more of the accompanying figures.

21. A reaction vessel having a closed lower end and an open upper end, the vessel comprising an integral condenser.

22. A vessel as claimed in claim 21 which is substantially tubular in form.

23. A vessel is claimed in claim 21 or 22 wherein the condenser comprises a double walled tubular section having an inlet and an outlet thorough which cooling fluid can flow passing through a cavity formed by said double walled section.

24. A vessel as claimed in any one of claims 21 to 23 having a connector portion forming the open upper end.

25. A vessel as claimed in any one of claims 21 to 24 formed entirely of glass

26. A vessel as claimed in any one of claims 21 to 25 comprising a ground glass connection forming the open upper end.

27. A vessel as claimed in any one of claim 21 to 26 having a substantially similar form to a test tube.

28. A vessel as claimed in any one of claim 21 to 27 comprising a head portion for mounting on the upper open end, said head portion having an inlet for receiving an inert gas.

29. A vessel as claimed in claim 28 wherein the head comprises an extension tube which, when the head is mounted on said upper opening, extends into the vessel.

30. A vessel as claimed in claim 28 or 29 wherein the head comprises a septa.

31. A vessel as claimed in claim 30 wherein the septa opens into the top of said extension tube permitting reagents to be added through the extension tube.

32. A vessel as claimed in any one of claims 28 to 31 wherein said head is made of glass.

33. A reaction vessel substantially as hereinbefore described with reference to, and/or as illustrated in one or more of the accompanying figures.

34. A reaction station comprising a reaction vessel as claimed in any one of claims 21 to 33.

Application No: GB 0016124.0 **Examiner:** R E Hardy
Claims searched: 1-20 **Date of search:** 24 October 2000

Patents Act 1977
Search Report under Section 17

Databases searched:

UK Patent Office collections, including GB, EP, WO & US patent specifications, in:

UK Cl (Ed.R): B1X (X18 X20 X8)

Int Cl (Ed.7): B01L (7/00 9/00 9/06)

Other: Online : EPODOC,WPI,JAPIO

Documents considered to be relevant:

Category	Identity of document and relevant passage		Relevant to claims
X Y	WO99/24160 A1	CHEMSPEED : Whole document	X:1,17 Y:2-7,9-12,14
Y	WO99/13988 A1	GLAXO : Whole document	3-6
X Y	WO98/57738 A1	CHEMSPEED : Whole document & note especially Figure 11	X:1,4-6,9,17 Y:2-7,9-12,14
Y	US5398806 A	QUINN : Whole document	2,4-7,9-12,14

X	Document indicating lack of novelty or inventive step	A	Document indicating technological background and/or state of the art.
Y	Document indicating lack of inventive step if combined with one or more other documents of same category.	P	Document published on or after the declared priority date but before the filing date of this invention.
&	Member of the same patent family	E	Patent document published on or after, but with priority date earlier than, the filing date of this application.